

# TMC114



## Drug Description

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TMC114 is a non-peptidic protease inhibitor (PI) containing 3(R),3a(S),6a(R)-bis-tetrahydrofuranyl urethane (bis-THF) and a sulfonamide isotere. [1]

## HIV/AIDS-Related Uses

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TMC114 is a PI that is highly active in vitro against both wild-type and PI-resistant HIV. TMC114 is being studied in combination with other antiretroviral medications for the treatment of HIV.[2]

## Pharmacology

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The pharmacokinetics of TMC114 have been studied in Phase II trials in healthy volunteers and in PI-experienced patients.

In healthy volunteers, TMC114 was rapidly absorbed; time to maximum plasma concentration (C<sub>max</sub>) was 3 hours. Steady-state concentrations were reached within 3 days. Increasing doses of TMC114 were administered alone and in combination with ritonavir (TMC114/r). TMC114/r had a more favorable pharmacokinetic profile compared to TMC114 alone. In the unboosted trial, C<sub>min</sub> at Day 14 ranged from 14 ng/ml to 142 ng/ml as the TMC114 dose increased. C<sub>max</sub> ranged from 2,168 ng/ml to 8,040 ng/ml. In the ritonavir-boosted trial, C<sub>min</sub> at Day 14 ranged from 480 ng/ml to 1,486 ng/ml and C<sub>max</sub> ranged from 1,569 ng/ml to 5,453 ng/ml.[3]

TMC114/r was administered to 50 multiple PI-experienced patients in a Phase IIa clinical trial. The median change in plasma HIV RNA (log<sub>10</sub>) from baseline to Day 14 was -1.24, -1.50, and -1.13 (TMC114/r dose 300/100 mg bid, 600/100 mg bid, and 900/100 mg bid, respectively). Ninety-seven percent of patients treated with TMC114/r had at least a 0.50 log<sub>10</sub> reduction from baseline.[4]

TMC114 is highly active against PI-resistant HIV isolates in vitro. In a study of 4,024 clinical HIV isolates, 80% of those isolates that were resistant to other PIs were susceptible to TMC114.[5]

## Adverse Events/Toxicity

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In clinical trials of TMC114, the most commonly reported adverse events were gastrointestinal (GI), skin, and central nervous system (CNS) disorders. The incidence of diarrhea, nausea, and vomiting was 78%, 15%, and 17%, respectively. TMC114 was formulated as a PEG-containing oral solution; GI side effects were attributed to the PEG solution. The incidence of headache was 22%. TMC114 boosted with ritonavir had a more favorable safety and tolerability profile than TMC114 alone. For TMC114/r, incidences of adverse events were diarrhea 30%, nausea 7.5%, headache 15%, and skin disorder 5%.[6]

One case of hepatitis has been reported in a patient taking TMC114 and five patients have experienced grade 3/4 hepatic enzyme elevation.[7]

## Clinical Trials

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For information on clinical trials that involve TMC114, visit the ClinicalTrials.gov web site at <http://www.clinicaltrials.gov>. In the Search box, enter: TMC114 AND HIV Infections.

## Dosing Information

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Mode of Delivery: Oral.[8]

## Other Names

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UIC96017[9]

UIC-94017[10]

## Further Reading

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Koh Y, Nakata H, Maeda K, Ogata H, Bilcer G, Devasamudram T, Kincaid JF, Boross P, Wang YF, Tie Y, Volarath P, Gaddis L, Harrison RW, Weber IT, Ghosh AK, Mitsuya H. Novel bis-tetrahydrofuranylurethane-containing nonpeptidic protease inhibitor (PI) UIC-94017 (TMC114) with potent activity against multi-PI-resistant human immunodeficiency virus in vitro. *Antimicrob Agents Chemother*. 2003

# TMC114



## **Further Reading (cont.)**

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## **Manufacturer Information**

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TMC114  
Tibotec  
Gen de Wittelaan L 11B 3  
2800 Mechelen  
Belgium

## **For More Information**

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Contact your doctor or an AIDSinfo Health Information Specialist:

- Via Phone: 1-800-448-0440 Monday - Friday, 12:00 p.m. (Noon) - 5:00 p.m. ET
- Via Live Help: [http://aidsinfo.nih.gov/live\\_help](http://aidsinfo.nih.gov/live_help) Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

## **References**

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1. Conf Retroviruses Opportunistic Infect. - 10th. February 2003. Abstract 553.
2. Conf Retroviruses Opportunistic Infect. - 10th. February 2003. Abstract 8.
3. Conf Retroviruses Opportunistic Infect. - 10th. February 2003. Abstract 549.
4. Conf Retroviruses Opportunistic Infect. - 10th. February 2003. Abstract 8.
5. International HIV Drug Resistance Workshop - 12th. June 2003. Abstract 17.
6. Conf Retroviruses Opportunistic Infect. - 10th. February 2003. Abstract 549.
7. Conf Retroviruses Opportunistic Infect. - 10th. February 2003. Abstract 8.
8. Conf Retroviruses Opportunistic Infect. - 10th. February 2003. Abstract 8.
9. Conf Retroviruses Opportunistic Infect. - February 2003. Abstract 553.
10. Antimicrob Agents Chemother - 2003 Oct;47(10):3123-9.